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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,829	04/14/2004	Nurith Kurn	492692001300	7311

25226 7590 04/21/2006

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EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,829	KURN ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-190* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42,46-60,62-79,81-103,105-142,146-165 and 167-190* is/are rejected.

7)☒ Claim(s) *43-45, 61, 80, 104, 143-145, and 166* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/9/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Upon further consideration, the restriction requirement issued December 5, 2005 is withdrawn. Claims 1-190 have been examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-42, 46-60, 62-79, 81-103, 105-142, 146-165, 170-176, 177-182, 183, 184, 185, 186, and 188 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurn (U.S. 6,251,639 A1) in view of Lizardi (U.S. 6,124,120).

With regard to Claims 1, 49, 65, 84, 108, and 149, Kurn teaches a method for amplification of a template polynucleotide (Figure 1; Column 4, Lines 25-45, for example): (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion (Columns 18-20, for example); (b) extending the composite primer with DNA polymerase (Column 25, Lines 30-67, for example); (c) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid (Column 26, Lines 10-25, for example) such that another composite primer can hybridize to the template and repeat primer extension by strand displacement, whereby multiple copies of the complementary sequence of the target sequence are produced (Figure 1; Column 29, for example). Kurn does not expressly disclose an initial template nucleic acid replication reaction incorporating a random set of primers capable of hybridizing to a multiplicity of template polynucleotide sites.

Lizardi teaches a whole genome strand displacement amplification (WGSDA) reaction comprising (Figure 2; Columns 8,9, for example): (a) mixing a set of random or partially random primers with a genomic sample (or other nucleic acid sample of high complexity), to produce a primer-target sample mixture, and incubating the primer-target sample mixture under conditions that promote hybridization between the primers

and the genomic DNA in the primer-target sample mixture, and (b) mixing DNA polymerase with the primer-target sample mixture, to produce a polymerase-target sample mixture, and incubating the polymerase-target sample mixture under conditions that promote replication of the genomic DNA. Lizardi further discloses several advantages of their methods including the ability to synthesize multiple overlapping copies of the entire genome in a short time (Abstract; Column 3, Lines 45-67, for example). Lizardi clearly demonstrates an initial template nucleic acid replication reaction incorporating a random set of primers capable of hybridizing to a multiplicity of template polynucleotide sites.

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate an initial template nucleic acid replication reaction incorporating random set of composite primers comprising an RNA portion and a 3' DNA portion capable of hybridizing to a multiplicity of template polynucleotide sites since Lizardi expressly suggests such a modification for the purposes of whole genome amplification in a short time.

With regard to Claims 2, 3, 22, 23, 53, 54, 69, 70, 88, 89, 90, 92-97, 114, 115, 117, 118, 120-123, 151, and 153-158, Kurn discloses reverse transcriptase and combinations of thereof with DNA polymerases (Column 16, Lines 45-65; Columns 25,26, for example).

With regard to Claims 4, 5, 20, 124, and 125, the use of random primers (Lizardi, Column 9, for example) encompasses the initial replication primer and subsequent amplification primer being the same and/or different.

With regard to Claims 6, 7, 17-19, 24, 51, 52, 67, 68, 91, 116, and 152, Kurn discloses the addition of RNaseH (Column 26, Lines 10-25, for example).

With regard to Claims 8-10, 25, 26, 50, 66, 73, 85-87, 126, and 150, the instant specification states, "as used herein, "auxiliary primers" refers to a population of random and/or partially randomized primers." Thus, as discussed above, Lizardi clearly demonstrates an initial template nucleic acid replication reaction incorporating a random set of primers capable of hybridizing to a multiplicity of template polynucleotide sites.

With regard to Claims 11, 72, and 109, Kurn discloses a DNA template (Column 16, Lines 45-65, for example).

With regard to Claims 12-14 and 110-112, Lizardi discloses a plurality of random/different primers (Column 9, for example).

With regard to Claims 15, 16, 71, and 113, Kurn discloses an mRNA template (Column 16, Lines 45-65, for example).

With regard to Claims 11, 72, and 109, Kurn discloses a DNA template (Column 16, Lines 45-65, for example).

With regard to Claim 21, Lizardi discloses the subsequent addition of primers for amplification (Figure 2; Columns 8,9, for example).

With regard to Claims 27-34, 55, 56, 98, 99, 128-135, 160, and 161, Kurn discloses composite primers comprising a 5' RNA portion and a 3' DNA portion (Columns 18-20, for example).

With regard to Claims 35-42, 57-60, 100-103, 136-142, and 162-165, Kurn discloses composite primers comprising the recited nucleotide construction (Columns 18-20, for example).

With regard to Claims 35-42, 57-60, 100-103, 136-142, and 162-165, Kurn discloses composite primers comprising the recited nucleotide construction (Columns 18-20, for example).

With regard to Claims 46, 47, 62, 63, 81, 82, 105, 106, 146, 147, 167, and 168, Kurn discloses any base variation of nucleotide (Column 13, for example).

With regard to Claims 48, 64, 107, 148, and 169, Kurn discloses labeled nucleotides (Column 35, Lines 40-55, for example).

With regard to Claims 170-176, Kurn discloses methods of making an array, (Column 7, Lines 40-50; Column 39, Lines 40-60, for example).

With regard to Claims 177-182, Kurn discloses methods of characterizing a nucleic acid (Column 40, Lines 1-50, for example).

With regard to Claims 183 and 184, Kurn discloses methods of quantification gene expression (Column 40, Lines 1-50, for example).

With regard to Claim 185, the amplification methods of Kurn and Lizardi inherently create libraries of polynucleotide amplification products (Kurn, Column 48, Example 4, for example).

With regard to Claim 186, Kurn discloses hybridizing a polynucleotide amplification product comprising multiple copies of target polynucleotide to a polynucleotide population (Column 53,54, Example 10, for example).

With regard to Claim 188, absent of any formal definition of the term "storing", the term is has been interpreted to encompass any amount of time after amplification. Kurn discloses the storage of polynucleotide amplification product between amplification and gel electrophoresis analysis (Column 46, Lines 15-25, for example).

With regard to Claims 189 and 190, Kurn discloses kits composite primer comprising an RNA portion and a 3' DNA portion. It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to create a kit of random composite primers comprising an RNA portion and a 3' DNA portion capable of hybridizing to a multiplicity of template polynucleotide sites since Lizardi expressly suggests such a modification for the purposes of whole genome amplification in a short time.

2. Claim 187 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kurn (U.S. 6,251,639 A1) in view of Lizardi (U.S. 6,124,120), in further view of Malek et al. (U.S. 5,712,127).

With regard to Claim 187, the methods of Kurn and Lizardi have been outlined in the above rejections. Neither Kurn nor Lizardi expressly disclose differential amplification by hybridizing a DNA driver polynucleotide population to a RNA population.

Malek et al. disclose an amplification method comprising: hybridizing a DNA driver polynucleotide population to a RNA population, whereby a subpopulation of the

RNA population forms a complex with the driver population (Column 4, Lines 25-35, for example); cleaving RNA with an agent that cleaves RNA in an RNA/DNA heteroduplex (Column 4, Lines 55-65). Malek expressly discloses the method as able to preferentially amplify target sequences (Column 4, Lines 20-25, for example). Malek further discloses several advantages of the methods including the ability to avoid the physical removal of hybridized sequences before amplification (Column 4, Lines 5-10, for example).

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate an initial sequence selection reaction into the methods of Kurn and Lizardi since Malek expressly suggests such a modification for the selection of desired sequences and the added ability to avoid the physical removal of hybridized sequences before amplification.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It is noted that only representative claims will be discussed.

1. Claims 1 and 189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 9 and 266 of Kurn (U.S. Patent No. 6,946,251 B2).

Claim 9 of Kurn ('251) recites a method of generating multiple copies of a polynucleotide sequence complementary to an RNA sequence of interest, said method comprising the steps of: (a) extending a first primer hybridized to a target RNA with at least one enzyme comprising RNA-dependent DNA polymerase activity, wherein the first primer is a composite primer comprising an RNA portion and a 3' DNA portion, whereby a complex comprising a first primer extension product and the target RNA is produced; (b) cleaving RNA in the complex of step (a) with at least one enzyme that cleaves RNA from an RNA/DNA hybrid; (c) extending a second primer hybridized to the first primer extension product with at least one enzyme comprising DNA-dependent DNA polymerase activity and at least one enzyme comprising RNA-dependent DNA polymerase activity, whereby a second primer extension product is produced to form a complex of first and second primer extension products; (d) cleaving RNA from the first primer in the complex of first and second primer extension products with at least one

enzyme that cleaves RNA from an RNA/DNA hybrid such that a composite amplification primer hybridizes to the second primer extension product, wherein the composite amplification primer comprises an RNA portion and a 3' DNA portion; (e) extending the composite amplification primer hybridized to the second primer extension product with at least one enzyme comprising DNA-dependent DNA polymerase activity; whereby said first primer extension product is displaced, RNA is cleaved from the composite amplification primer and another composite amplification primer hybridizes such that primer extension and strand displacement are repeated, and whereby multiple copies of a polynucleotide sequence complementary to the RNA sequence of interest are generated, wherein the first primer comprises a random primer sequence.

Furthermore, Claim 266 of Kurn recites a kit for amplifying a target RNA, comprising a first composite primer and a second composite primer, wherein the first composite primer comprises an RNA portion and a 3' DNA portion, wherein the second composite primer comprises an RNA portion and a 3' DNA portion, and wherein the second composite primer comprises a sequence that is hybridizable to a polynucleotide comprising a complement of the first composite primer, wherein the 3' DNA portion of the first composite primer comprises a random primer sequence.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive method and kit thereof. The above Kurn ('251) recites a species of the genus method recited in the instant claim. The disclosure of a species renders the genus method obvious over Kurn ('251).

2. Claims 1 and 189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 and 77 of Kurn (U.S. Patent No. 6,692,918 B2) in view of in view of Lizardi (U.S. 6,124,120).

Claim 1 of Kurn ('918) recites a method for amplifying a polynucleotide sequence complementary to a target polynucleotide sequence comprising: (a) extending a composite primer in a complex comprising (i) a DNA template strand comprising the target sequence; and (ii) the composite primer, said composite primer comprising an RNA portion and a 3' DNA portion, wherein the DNA template strand is hybridized to the composite primer; (b) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such tat another composite primer hybridizes to the template and repeats primer extension by strand displacement, whereby multiple copies of the complementary sequence of the target sequence are produced.

Furthermore, Claim 77 of Kurn ('918) recites a kit for amplifying a polynucleotide sequence, comprising a composite primer, wherein the composite primer comprises an RNA portion and a 3' DNA portion, and wherein the RNA portion of the composite primer consists of about 5 to about 25 nucleotides and the DNA portion of the composite primer consists of about 3 to about 12 nucleotides.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive method and kit thereof with a *prima facie* obvious modification.

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate an initial template nucleic acid replication reaction incorporating random set of composite primers comprising an RNA portion and a 3' DNA portion capable of hybridizing to a multiplicity of template polynucleotide sites since Lizardi expressly suggests such a modification for the purposes of whole genome amplification in a short time.

3. Claims 1 and 189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 and 49 of Kurn (U.S. Patent No. 6,251,639 B2) in view of in view of Lizardi (U.S. 6,124,120).

Claim 1 of Kurn ('251) recites a method for amplifying a polynucleotide sequence complementary to a target polynucleotide sequence comprising: (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) optionally hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template; (c) extending the composite primer with DNA polymerase; (d) cleaving the

RNA portion of the annealed composite with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer hybridizes to the template and repeats primer extension by strand displacement, whereby multiple copies of the complementary sequence of the target sequence are produced.

Furthermore, Claim 77 of Kurn ('251) recited a kit for amplification of a target polynucleotide sequence, comprising (a) a composite primer comprising a 3' DNA portion and an RNA portion, and (b) a polynucleotide comprising a termination polynucleotide sequence, wherein the termination polynucleotide sequence effects cessation of DNA replication of a template by DNA polymerase.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to the same general inventive method and kit thereof with a *prima facie* obvious modification.

It would have been *prima facie* obvious to a practitioner of ordinary skill in the art at the time of invention to incorporate an initial template nucleic acid replication reaction incorporating random set of composite primers comprising an RNA portion and a 3' DNA portion capable of hybridizing to a multiplicity of template polynucleotide sites since Lizardi expressly suggests such a modification for the purposes of whole genome amplification in a short time.

Allowable Subject Matter

Claims 43-45, 61, 80, 104, 143-145, and 166 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

A sequence search of the pertinent databases revealed no prior art teaching or fairly suggesting the use of primers having the sequences contained in SEQ ID NOs: 1 and 2.

Conclusion

Claims 1-42, 46-60, 62-79, 81-103, 105-142, 146-165, 167-190 are rejected.

Claims 43-45, 61, 80, 104, 143-145, and 166 are objected to.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4/14/06

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4/17/06